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<p>(54) Title: ASSEMBLY OF POLYTHIOPHENE DERIVATIVE ON A SELF-ASSEMBLED MONOLAYER (SAM)</p> <div data-bbox="454 1155 1104 1701"> <p>The figure is a line graph showing Absorbance on the y-axis (ranging from 0.0 to 0.8) versus Wavelength (nm) on the x-axis (ranging from 300 to 800). There are approximately 10 curves stacked vertically, each showing a broad absorption peak between 450 nm and 550 nm. An inset in the upper right of the graph area shows a chemical structure of a polythiophene derivative with a sulfonic acid group (-SO₃H) and an amine group (-NH₂) attached to the thiophene ring. The structure is shown reacting with H₂N-CH₂-CH₂-CH₂-CH₂-NH₂.</p> </div> <p>(57) Abstract</p> <p>A method for obtaining solid-state devices, through the deposition of monolayers of polythiophenes with the use of amine-bearing self-assembled monolayers (SAMs), a strong complex being formed between the remaining sulfonic acid groups with adequately chosen substituents. Functionalized electroactive substrates can be easily obtained which can be used to carry out a variety of subsequent reactions and can display interesting recognition for field-responsive features. This methodology based on supramolecular polymeric assemblies can find many applications in the areas of sensors, diagnostics, therapeutics and drug screening.</p>		

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TITLE OF THE INVENTION

ASSEMBLY OF POLYTHIOPHENE DERIVATIVE ON A SELF-ASSEMBLED MONOLAYER (SAM)

5 FIELD OF THE INVENTION

The present invention relates to a methodology based on supramolecular polymeric assemblies for use in the areas of sensors, diagnostics, therapeutics and drug screening.

10

BACKGROUND OF THE INVENTION

The search for smart materials is an exploding research field due to the high demand for materials capable of carrying out increasingly complex tasks and performing various functions. In this respect, functionalized regioregular π -conjugated polythiophenes are a very promising class of material exhibiting impressive chromic responses upon exposure to specific stimuli, opening the way to the design of a variety of sensory devices.

20

For instance, these polymers, bearing adequately designed side chains, can undergo striking conformational changes when exposed to heat, light or various chemical and biochemical moieties giving rise to thermochromism, photochromism, ionochromism, or even biochromism.

25

These optical transitions, from deep violet to (maximum of absorption around 550 nm) to bright yellow (maximum of absorption

near 400 nm) are believed to be related to a planar to non-planar (from highly conjugated to less conjugated) conformational transition of the backbone.

5 Indeed, in conjugated polymers, there is a strong correlation between the electronic structure and the backbone conformation leading to a modification of the effective conjugation length associated with a shift of the absorption in the UV-visible range.

10 Studies on different polythiophene derivatives have suggested that this conformational modification of the main chain could be driven by order-disorder transitions of the side chains. However, all these studies on polythiophene derivatives demonstrated that the detection or recognition event is mainly a function of the nature and characteristics
15 of the side chains, requiring the cumbersome design, synthesis, and purification of numerous monomeric and polymeric derivatives.

 Similar findings resulted from the study of functionalized π -conjugated polydiacetylene and α -conjugated polysilanes.

20 Well known also are self-assembled monolayers of alkanethiolates on gold or alkanesiloxanes on glass as they have been the subject of intensive research during the recent years. Such monolayers have attracted a lot of attention as potential building blocks
25 for supramolecular assemblies with new engineered chemical and optical properties.

OBJECTS OF THE INVENTION

5 An object of the present invention is therefore to introduce the required side chains on the polymers through the use of acid-base interactions.

10 A further object of the present invention is to open the way to a whole novel area of surface modification through the use of electrostatic interactions.

15 A further object of the present invention is to provide a novel and simple way to create potential building blocks for supramolecular assemblies with new engineered chemical and optical properties

SUMMARY OF THE INVENTION

20 More specifically, in accordance with the present invention, there is provided a novel family of materials consisting of complexes of polythiophene derivatives, bearing sulfonic acid moieties, and one or several amine containing molecules designed by taking advantage of the electrostatic interactions between the complementary
25 charged moieties.

Indeed, the present invention takes advantage of the fact that poly(2-(4-methyl-3-thienyloxy)ethanesulfonic acid) can react with

various basic molecules to yield tunable, functionalized (through electrostatic interactions), and chromic polymers. New responsive polymers, both in solution and in the solid state, can then be easily prepared and utilized to detect a large number of different and targeted external stimuli.

Interestingly, these polymers bearing electrostatically bound substituents, in addition to being facile and straightforward to obtain, have been found to possess similar characteristics to those having covalently bound substituents.

For instance, aqueous solutions of sodium poly(2-(4-methyl-3-thienyloxy)-ethanesulfonate) undergo a thermally induced violet-to-yellow color (a shift of the absorption maximum from 540 nm to 400 nm) transition, which is believed to be related to a rod-to-coil (planar to non planar) conformational transition of the conjugated backbone.

Upon electrostatic neutralization of poly(2-(4-methyl-3-thienyloxy)-ethanesulfonic acid) with different amine-bearing moieties, the thermochromic behavior observed upon heating of the neutral solutions (Figure 2) revealed a decrease of the 540 nm absorption band and the apparition of a new band around 400 nm with the accompanying color changes from violet to yellow.

This thermochromic feature is similar to that observed for the polymeric sodium salt, but the temperature range of the chromic transition was found to be strongly dependent on the nature of the substituents. Indeed, the increase of the bulkiness of the electrostatically

bound substituents seems to disrupt more easily the planar polythiophene assemblies (Figure 2, inset).

5 The highly conjugated (violet) form is believed to be associated with intermolecular and intramolecular (through chain folding) aggregates, while upon heating, side-chain disordering disrupts these assemblies to yield nonplanar (less conjugated) polymer chains. A similar cation size-dependant chromaticity has been recently reported with salts involving regioregular poly(thiophene-3-propionic acid) and could be
10 explained by a similar sterically induced disruption of the aggregated phase.

 These properties may lead to a variety of applications such as information storage, electroluminescent devices, optical signal
15 processing, solar energy conversion, electrochemical cells, EMI shieldings, antistatic coatings, bioelectronic devices, etc.

 For instance, polyoxyethylene substituents give rise to ionochromism, while azobenzene result in photochromic materials and
20 biotinylated derivatives were used to detect the well-known avidin molecule.

 The neutralization of the acid form can be monitored optically in real time through the decrease of the 800 nm absorption band,
25 characteristic of an oxidized sulfonic acid-bearing polymer. Successive additions of different amine-bearing molecules result in multi-functionalized polymeric chains.

In addition, self assembled monolayers (SAM) of amine functionalized alkanethiolates or alkanesiloxanes can be modified by polythiophenes through complexation with the side-chain acid moieties. A complex is formed between the sulfonic acids of the polymer and the amine groups of the SAMs. By pre-neutralizing some of the sulfonic acid groups with adequately chosen substituents, functionalized substrates can be obtained which can be used to carry out a variety of subsequent reactions and can display interesting recognition or affinity features.

In addition to the use of colorimetric detection, due to the change in the absorption characteristics of the polymer backbone, electrochemical techniques can also be advantageously employed.

The recognition or binding events, between the functionalized side chains and the external stimuli, could be detected and measured by taking advantage of the large difference in the electronic structure between the planar and non planar forms of the polymer backbone, which results in significant shift of the oxidation potentials, allowing the design of highly selective and efficient, versatile and tunable electrochemical devices.

For instance, the oxidation potential of poly((3-(2-methyl-1-butoxy)-4-methylthiophene), a polythiophene derivative that is stable in both its coiled (yellow) and planar (violet) form, is found to be drastically different depending on its conformational state. When the non-planar form is oxidized, a potential of +0.88 V vs SCE is obtained while the planar form is oxidized at around +0.70 V. This huge difference, associated with the fact that the rod-to-coil transition can be induced by several external

stimuli, allow the design of highly selective and easily obtainable solid-state electrochemical detection devices.

5 The cumbersome multi-step synthesis of functional polythiophene derivative can be advantageously replaced by electrostatically binding an adequately functionalized derivative.

10 Other objects, advantages and features of the present invention will become more apparent upon reading of the following non restrictive description of preferred embodiments thereof, given by way of example only with reference to the accompanying drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

15 In the appended drawings:

20 Figure 1 is a UV visible absorption spectra of an aqueous solution of poly(2-(4-methyl-3-thienyloxy)ethanesulfonic acid) ($\sim 10^{-4}$ M) upon addition of *n*-butylamine, at room temperature;

25 Figure 2 is a temperature-dependant UV-visible absorption spectra of the 1:1 complex between *n*-butylamine and poly(2-(4-methyl-3-thienyloxy)ethanesulfonic acid) in water. Evolution of the relative absorbency at 540 nm as a function of the temperature for (a) sodium poly(2-(4-methyl-3-thienyloxy)ethane sulfonate), (b) butylammonium poly(2-(4-methyl-3-thienyloxy)ethanesulfonate) and (c) tetrabutylammonium poly(2-(4-methyl-3-thienyloxy)ethane sulfonate);

Figure 3 is a UV-visible absorption spectra of the 1:1 complex between biocytinhydrazide and poly(2-(4-methyl-3-thienyloxy)ethanesulfonic acid) ($\sim 5 \times 10^{-7}$ mol) as a function of the addition of avidin, in water/methanol (98:2, v/v);

5

Figure 4 is a schematic description of the modified electrode;

Figure 5 is a cyclic voltammogram of a monolayer deposited on an aminosilane-treated ITO electrode of (a) poly(2-(4-methyl-3-thienyloxy)ethanesulfonic acid), (b) a 0.5:1 complex between biocytinhydrazide and poly(2-(4-methyl-3-thienyloxy)ethanesulfonic acid), and (c) a 0.5:1 complex between biocytin hydrazide and poly(2-(4-methyl-3-thienyloxy)ethanesulfonic acid) dipped into an aqueous avidin solution. All cyclovoltammograms have been recorded in acetonitrile with 0.1 M of tetrabutylammonium tetrafluoroborate at a scan rate of 100 mV/s vs Ag/AgCl; and

Figure 6 is a cyclic voltammogram and UV-visible absorption spectrum of cast films of poly(3-(2-methyl-1-butoxy)-4-methylthiophene in (1) a highly conjugated form and (2) a less conjugated form. All cyclovoltammograms have been recorded in acetonitrile with 0.1M of tetrabutylammonium tetrafluoroborate at a scan rate of 100mV/s vs Ag/AgCl.

25

DESCRIPTION OF THE PREFERRED EMBODIMENT

Chromic behaviour was found in poly(2-(4-methyl-3-thienyloxy)ethanesulfonic acid) neutralized by sodium hydroxide. This polymer exhibit, upon heating in water, a purple-to-yellow color transition related to a rod-to-coil transition of the conjugated backbone, with the
5 absorption band at 540 nm decreasing while a new absorption band at 420 nm is appearing.

Similarly upon heating, poly(2-(4-methyl-3-thienyloxy)ethanesulfonic acid) neutralized by n-butylamine (or various
10 other amine derivative such as tetrabutylammonium bromide) are found to behave in a comparable manner, however a noticeable difference in the temperature range of the rod-to-coil transition. Simple acid-base chemistry has thus been used to introduce a variety of substituents which otherwise would require many synthetic and purification steps.

15 For instance, the absorption bands at 540 and 580 nm are still visible, even at 100°C, in the case of the polymer neutralized by sodium hydroxide while in the two other cases these bands have almost disappeared around 70-80°C. The evolution of the absorption at 540 nm
20 as a function of temperature reveals a significant difference between the behavior of the different polymers, with a very significant and rapid depletion of the 540 nm band in the case of the tetrabutylammonium substituents. The introduction of such a bulky substituents induces a more facile disruption of the planar conformation compared to the two
25 other cases.

In addition to the modulation of the chromic characteristics of the electrostatically modified polythiophenes, a whole

series of functional substituents can be easily introduced on the polymeric backbone and combine the inherent chromic properties of this latter with the affinity and/or recognition properties of adequately selected substituents.

5

Self-acid doped poly(2-(3-thienyloxy)ethane sulfonate)s and poly(2-(4-methyl-3-thienyloxy)ethanesulfonic acid) exhibits a large absorption band around 800 nm, characteristic of an oxidized and conducting (S S/cm) form.

10

Stepwise addition of sodium hydroxide aliquots leads to a progressive neutralization of the polymer, with the neutral and insulating ($< 10^{-6}$ S/cm) polymeric salt showing a very different absorption spectrum (maximum of absorption at 540 nm instead of 800 nm), from pale grey to deep violet.

15

This self-acid-doping process is fully reversible by the neutralization of the acid moieties by sodium hydroxide solution. The absorption at 800 nm is decreasing with the addition of increasing amount of sodium hydroxide allowing real time monitoring of the neutralization process and hence modulation of the properties and characteristics of the resulting polymers.

20

In addition to the modulation of the thermochromic characteristics of polythiophenes through the tuning of the electrostatically attached substituents, various functional substituents can be easily attached to the polythiophene backbone combining the inherent chromic properties of the latter species with the affinity and/or recognition

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properties of adequately selected substituents, opening the way to the fabrication of integrated chemical systems which incorporate both a trigger and a transducer.

5 For example, the synthesis of a water-soluble
biochromic derivative has been previously obtained through the covalent
attachment of biotin to a thiophene copolymer, containing randomly
distributed sodium sulfonate and biotin terminal groups. The addition of
avidin, well known for its very strong interaction with biotin, resulted in a
10 sharp color change of the polymer solution. The tedious multi step
synthesis of the biotinylated polythiophene derivative can be
advantageously replaced by the electrostatic binding of an adequately
functionalized biotin derivative (i.e. biocytin hydrazide, an amine
functionalized biotin derivative) to poly(2-(4-methyl-3-thienyloxy)-
15 ethanesulfonic acid).

In a preferred embodiment therefore, water-soluble
polythiophene derivative, bearing a biotin molecule, can be synthesized
through the electrostatically binding of biotin to a thiophene polymer,
20 containing sulfonic acid groups.

The addition of avidin resulted in a sharp color change
(from yellow to deep purple) due to an important coil-to-rod transition
induced by the introduction of the huge avidin. (in this case biocytin, an
25 amine-terminated and highly water-soluble biotin derivative) to poly(2-(4-
methyl-3-thienyloxy)ethanesulfonic acid).

A deep purple solution was obtained with its main absorption around 530 nm and, by adding a few percent of a co-solvent (methanol, ethanol, tetrahydrofuran,...), the main absorption can be tuned at will. The solution composition is adjusted in such a way that the main
5 absorption is around 400 nm, indicating that the main chains are predominantly in the coiled form (a similar effect can be obtained in pure water by increasing the temperature).

Upon the addition of aliquots of aqueous avidin, a
10 progressive decrease of the 400 nm absorption band is observed, while a new band, centered around 500 nm, is appearing (figure 3). This represents a colour shift from yellow to violet. The addition of avidin seems to induce some kind of rigidification of the polymeric chains, that can be related to the fact that four binding sites are present on each
15 avidin, each being able to interact with a nearby biotin with as a result possible cross-linking.

The change in the absorption characteristics (both the depleting and the growing bands) are found to be linear with increasing
20 avidin amounts, opening the way to the design of simple and affordable biochromic sensory devices.

In contrast, in the case of random copolythiophene with covalently bound avidin, avidin binding induced a disordering of the
25 polythiophene backbone (formation of the coil conformation).

The difference between these two systems may be due to the different density and distribution of the binding moieties, multiple

bindings to avidin creating a rigidification of the polythiophene backbone and a single binding leading to a coil conformation.

5 Indeed, a violet precipitate was also observed in the present study but after two or three days. Moreover the fact that an isosbestic point is also present in this conformational transition of the conjugated backbones indicates also a cooperative mechanism where the twisting of a first unit seems to induce the twisting of a series of neighboring units.

10

This phenomenon has always been found with regioregular chromic polythiophenes and involves therefore an amplification (at least a factor of 100, here) of the detection. The absorption characteristics vary linearly with increasing avidin amounts (Figure 3, inset), opening the way to the design of simple biochromic sensory devices, with 10^{-9} to 10^{-13} mol detection ranges. With the present invention, above 10^{-8} mol avidin, the optical response is saturated.

15

20 Similarly, it has been shown that regioregular polythiophene derivatives bearing covalently attached oxyethylene oligomers can detect optically the presence of several alkali metal ions.

This characteristic can be duplicated with the electrostatic complexation of amino-oligo(oxyethylene) to the sulfonic acid polythiophene derivative.

25

In another preferred embodiment therefore, amino-polyoxyethylene is electrostatically complexed to sulfonic acid-bearing

polythiophenes to chromically detect the presence of several alkali metal ions. Upon the addition of increasing aliquots of potassium thiocyanate (KSCN), the main absorption band (540 nm) of the aqueous polymer solution decreases while a new band, around 400 nm, is appearing.

5

In an other preferred embodiment, photochromic polythiophenes is obtained through acid-base complexation with 4-phenylazolaniline. Upon irradiation, the predominantly *trans*-azobenzene side chains undergo an isomerization forcing the main polymeric chains to a rod-to-coil transition, in a manner similar to what has been observed in regioeregular polythiophenes covalently modified by azobenzene moieties.

10

In another preferred embodiment, the use of diaminated molecules permits to obtain positively charged polythiophenes derivatives, allowing the design of supramolecular assemblies through the alternate binding of oppositely charged moieties.

15

In an other preferred embodiment, poly(2-(4-methyl-3-thienyloxy)ethanesulfonic acid) can interact with silanized glass bearing terminal amine groups. Deposition of the polymer occurs with, as a direct consequence, the apparition of absorption bands in the range 450-500 nm. It has to be noticed that all the deposited polymer seems to be neutralized, with no more non-complexed sulfonic acid as evidenced by the complete disappearance of the 800 nm band. When a partially neutralized solution is used, a functionalized polythiophene monolayer electrostatically attached to the aminated substrate can be obtained .

20

25

The generality of the acid-base complexation reactions between poly(2-(4-methyl-3-thienyloxy)-ethanesulfonic acid) and amine-bearing molecules also opens the way to a novel area of surface modification through the use of electrostatic interactions.

5

Self-assembled monolayers of alkanesilanes on glass or alkanethiols on gold are now well known and have been the subject of intensive research activities during recent years. Moreover, such monolayers have attracted a lot of attention as potential building blocks for supramolecular assemblies with use of layer-by-layer deposition methods.

10

In a preferred embodiment therefore, by using a similar approach to that developed by Decher *et al.*, a silanized glass microscope slide bearing amino-terminal groups (using 3-aminopropyltrimetoxysilane) was dipped into an aqueous solution of poly(2-(4-methyl-3-thienyloxy)-ethanesulfonic acid).

15

Presumably, a monolayer of the oxidized self-acid-doped polymer is then transferred onto the substrate. An absorption band appears in the range of 500-550 nm, indicating an acid-base interaction (neutralization) between the amine-bearing substrate and the acidic polymer.

20

It has to be noticed that the absorbance² at 550 nm (0.002 per monolayer) of the resulting ultrathin polythiophene film is in the same range as that observed for a monolayer of a similar polymer (but in a nonplanar form, with a maximum of absorption near 400 nm) prepared

25

with the Langmuir- Blodgett technique, indicating that both techniques can be useful to obtain ultrathin (monolayer) polythiophene films with, obviously, different morphologies. Moreover, when a partially pre-neutralized polymer is used, a functionalized polythiophene monolayer
5 can be easily electrostatically bound to the amine-bearing substrate (Figure 4).

This easy process of attaching substituents and polymeric monolayers onto various substrates through the use of
10 electrostatic interactions allows the preparation of a large number of solid-state recognition/affinity sensors.

The deposition of monolayers is particularly critical for these solid state sensors since it is believed that the interaction between large biochemical
15 species and binding sites will mainly occur at the interface, and therefore, it is important to maximize the surface/volume ratio for such applications.

Moreover, due to the fact that these polythiophene derivatives are also electroactive, any perturbation in the conformation of
20 the main chain may result in a huge difference in the electronic structure of these materials and hence in their electrochemical properties.

For instance, a monolayer of poly(2-(4-methyl-3-thienyloxy)ethanesulfonic acid), has been deposited on a silanized ITO
25 glass bearing amine groups, and its cyclic voltammetry has been recorded and revealed an oxidation process around +0.88 V vs Ag/AgCl (Figure 5a). Upon deposition of a monolayer bearing biocytin hydrazide moieties, the oxidation peak remained around +0.90 V (Figure 5b) , while

the treatment of this modified electrode with avidin results in a 200 mV positive shift of the oxidation peak at +1.08 (Figure 5c). These results can be explained by a planar-to-nonplanar conformational transition of the polymeric backbone induced by the incorporation of the huge avidin, which is in agreement with the blue shift observed for the UV-visible absorption maximum.

Moreover, these electrochemical results with polythiophene monolayers are consistent with those obtained with cast films of poly(3-(2-methyl-1-butoxy)-4-methylthiophene) on platinum electrodes which can be obtained either in the yellow or violet form depending upon film preparation. The difference in the effective conjugation lengths also induces a 200 mV shift in the oxidation potential (Figure 6).

EXAMPLE 1

N-butylamine shows a marked pale grey-to-violet color transition with the decrease of the initial absorption band at 800 nm and the increase of a new band centered around 540 nm, indicating a progressive neutralization of the acidic and oxidized form with the concurrent formation of a neutral and amine-bearing polymeric material (Figure 1).

Experimental section

Material Sodium 2-(4-methyl-3 thienyloxy)ethanesulfonate and the corresponding polymer have been synthesized in known manner. The

sulfonic acid form of the polymer has been obtained by passing an aqueous solution of the sodium salt polymer through a strong cation (H⁺) exchange resin (Dowex HCR-W2) column. Amino-poly-(ethylene glycol) (amino-PEG)(Sherwater), *n*-butylamine, 4-phenyl-azolaniline, tetrabutylammonium tetrafluoroborate, tetrabutylammonium bromide, 3-aminopropyltrimethoxysilane (Aldrich), and biocytin and avidin (Pierce) were used as received. Neutralization of the sulfonic acid polymeric solution was usually carried out by the stepwise addition of aliquots of the various amine bearing molecules. Amino-functionalized silanized ITO-coated glass has been prepared following well established procedures. For instance, an ITO-coated glass (Applied glass) plate was dipped in a 70-30 H₂SO₄-H₂O₂ solution for 10 s in such a way as to enhance the hydrophilic nature of the surface to ensure the proper anchorage of the siloxane groups without destroying the conductive oxide layer. The glass plates are silanized by dipping them in a 5% solution of aminopropyl trimethoxysilane in toluene for various periods of time. For such a short silane derivative, a immersion time of 30 mn was found to be optimum in order to avoid the occurrence of multi layer deposition while obtaining an acceptable surface coverage. After several cycles of sonication and rinsing with fresh toluene, the glass plates were heated to 105°C for 1 h to allow the condensation reaction of the siloxane to proceed. The ITO electrodes were stored in dry argon prior to use. The electrostatic transfer of poly(2-(4-methyl-3-thienyloxy)ethanesulfonic acid) onto the ITO-coated glass slides was carried out by dipping the slides in a 0.01 M aqueous solution of the polymer. A 50 % pre-neutralization of the sulfonic acid polymer with biocytin hydrazide allows the transfer of biotinylated polythiophene onto amine-bearing silanized ITO-coated glass.

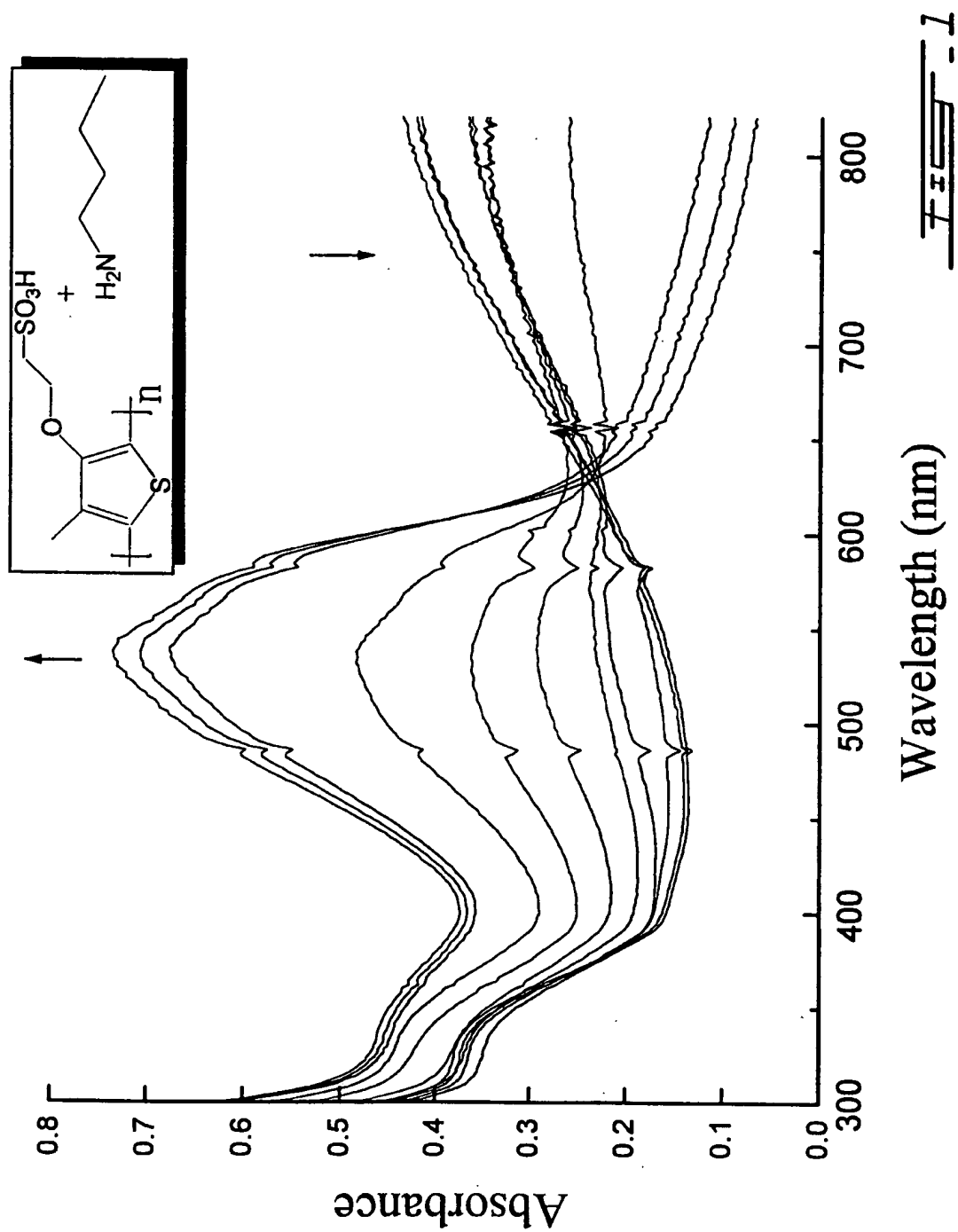
Experiment. UV-visible absorption spectra were obtained with a Hewlett-Packard diode array spectrophotometer (Model 8452A). Cyclic voltammetry measurements were obtained with a EG&G potentiostat/galvanostat (Model 273). Ag/AgCl reference electrode and platinum electrodes were used. Electrochemical measurements were performed at 100 mV/s with use of an electrolyte made of 0.1 M tetrabutylammonium tetrafluoroborate dissolved in acetonitrile. The silanized ITO-coated glass electrodes are dipped for various periods of time in different polymeric solutions. After copious rinsing to remove unbound polymeric chains and drying with dry argon, it was found that an immersion time of 1 min is sufficient to obtain reproducible cyclic voltammograms.

Although the present invention has been described herein above by way of preferred embodiments thereof, it can be modified, without departing from the spirit and nature of the subject invention as defined in the appended claims.

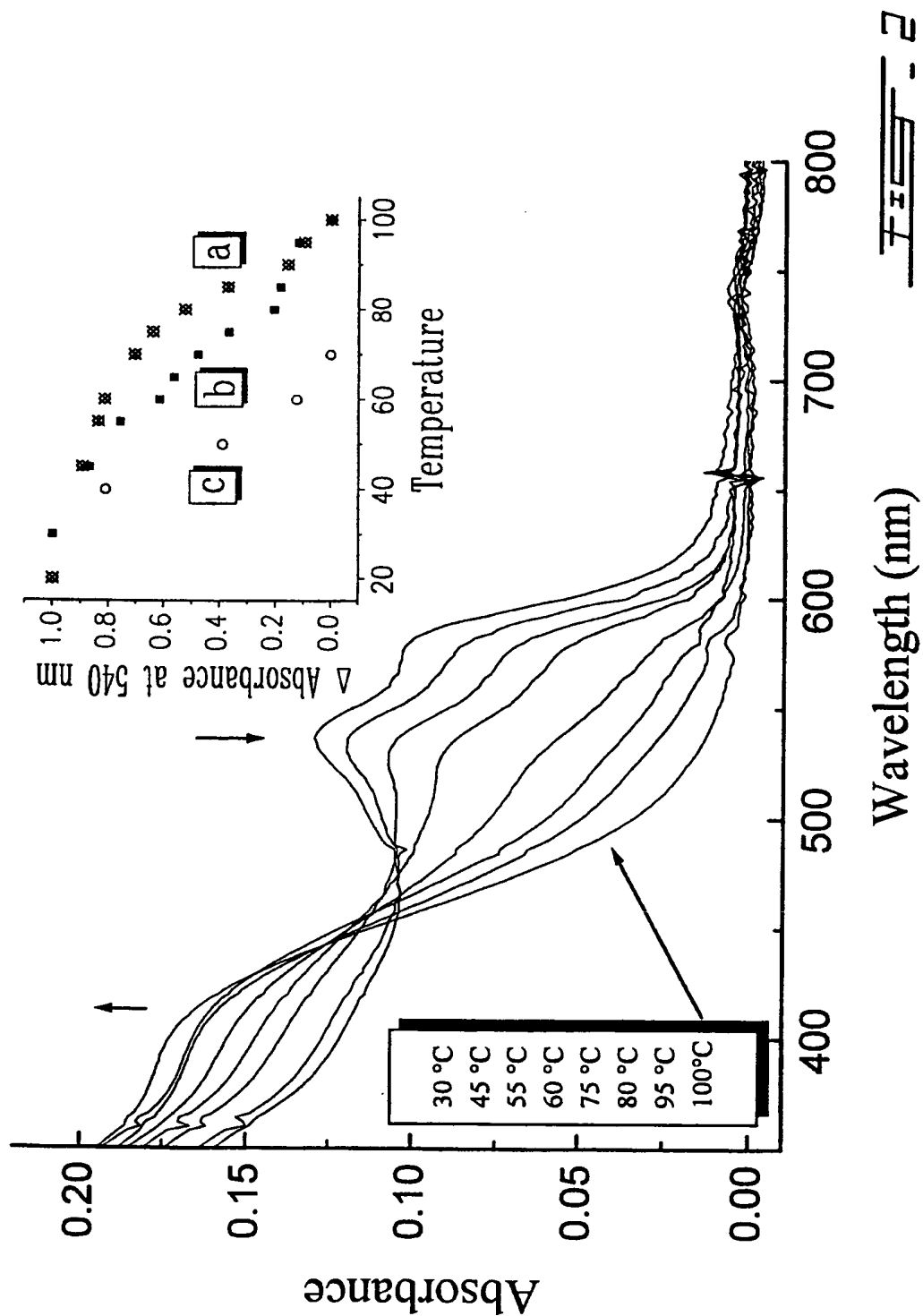
WHAT IS CLAIMED IS:

- 5 1. A method for depositing monolayers of
polythiophenes comprising the steps of:
- a) using aminated self-assembled monolayers (SAMs) of substances
 chosen from the group of substances comprising alkanethiolates on gold
 and alkanesiloxanes on glass;
- 10 b) forming a complex between the sulfonic acids of the polymer and the
 amine groups of the SAMs;
- c) preneutralizing some of the sulfonic acid groups with adequately
 chosen substituents;
- 15 d) obtaining functionalized substrates capable of recognition or affinity
 features.
2. The product obtained by the method of claim 1.

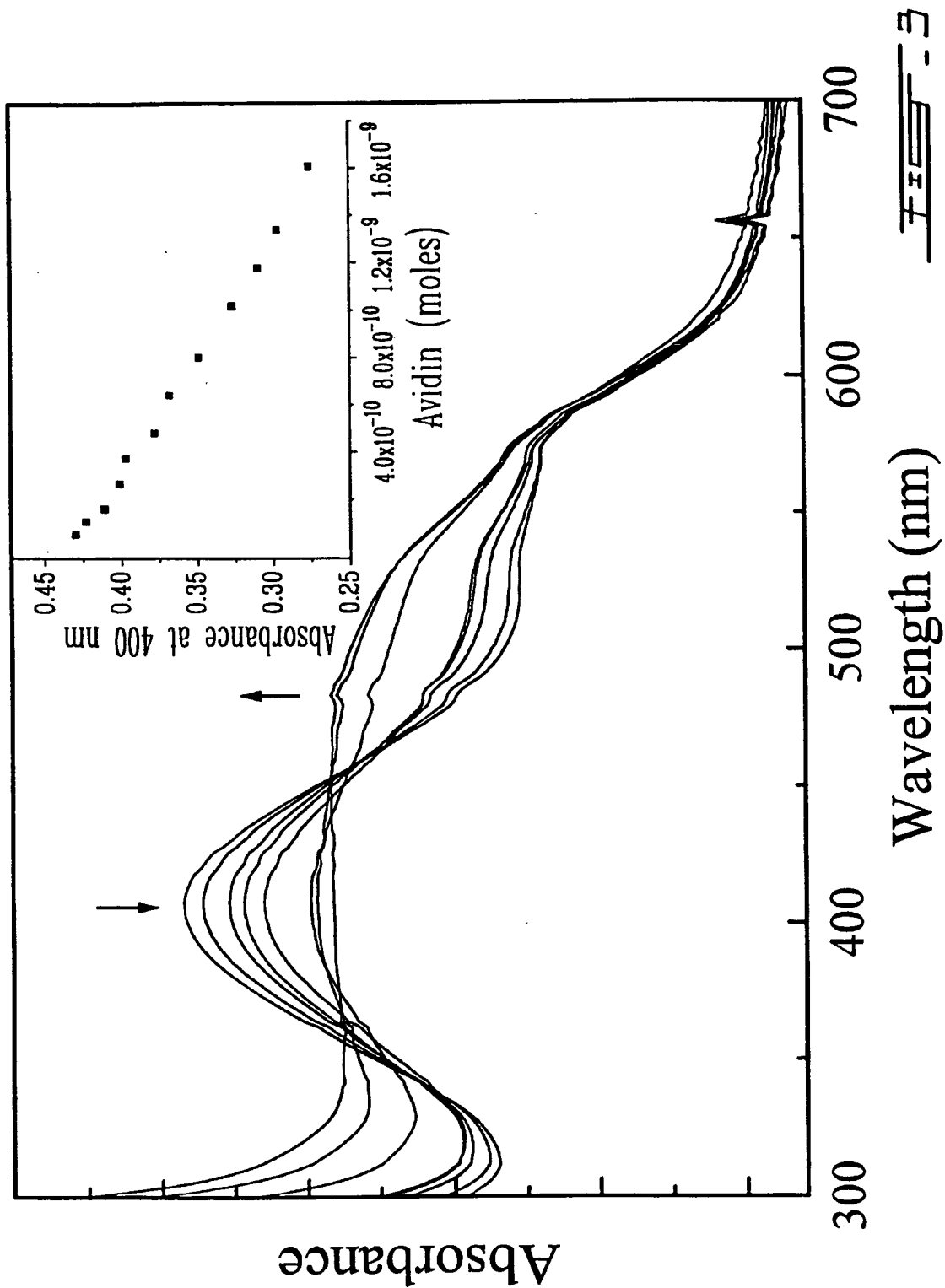
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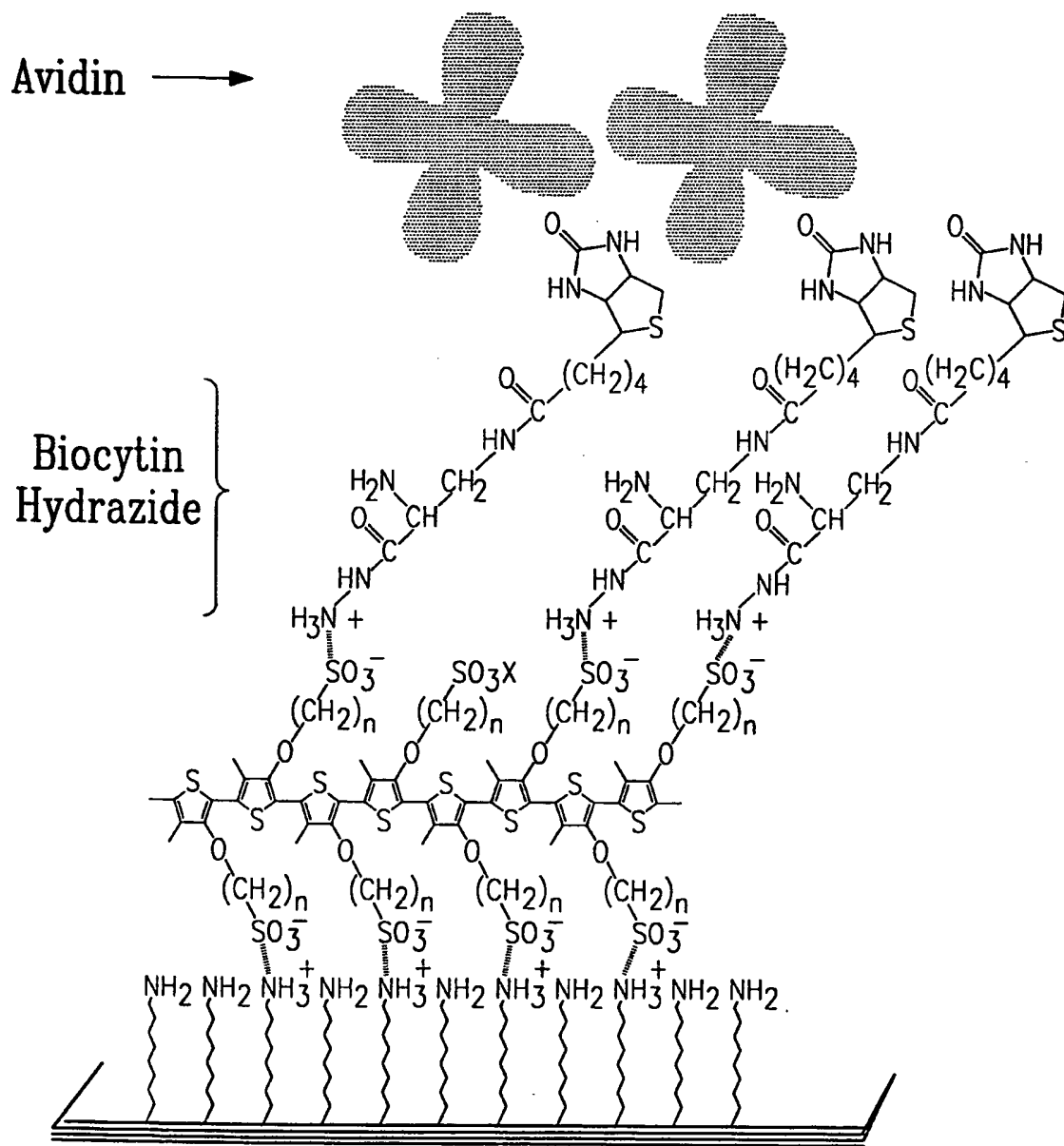
2/6



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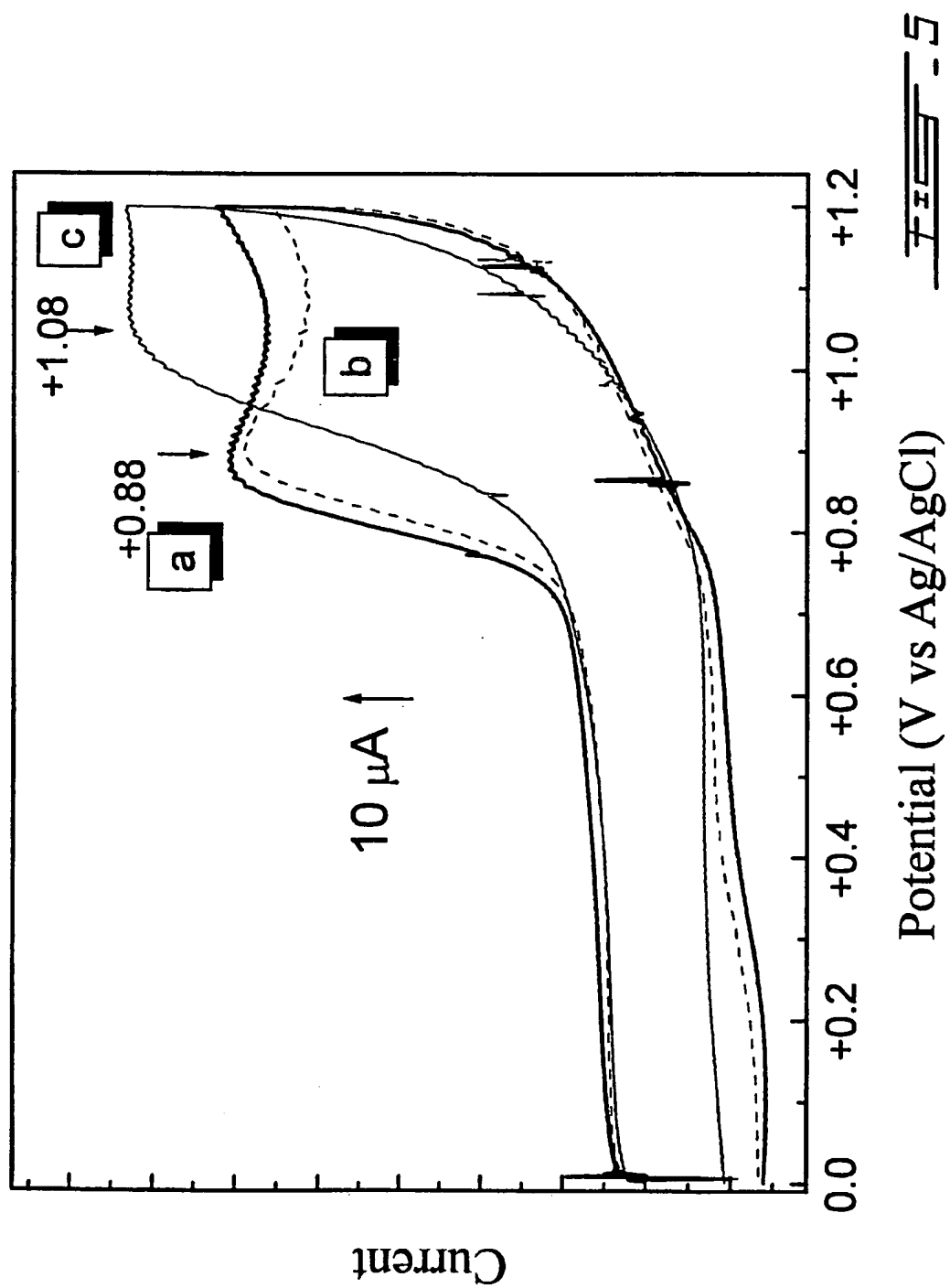
4/6



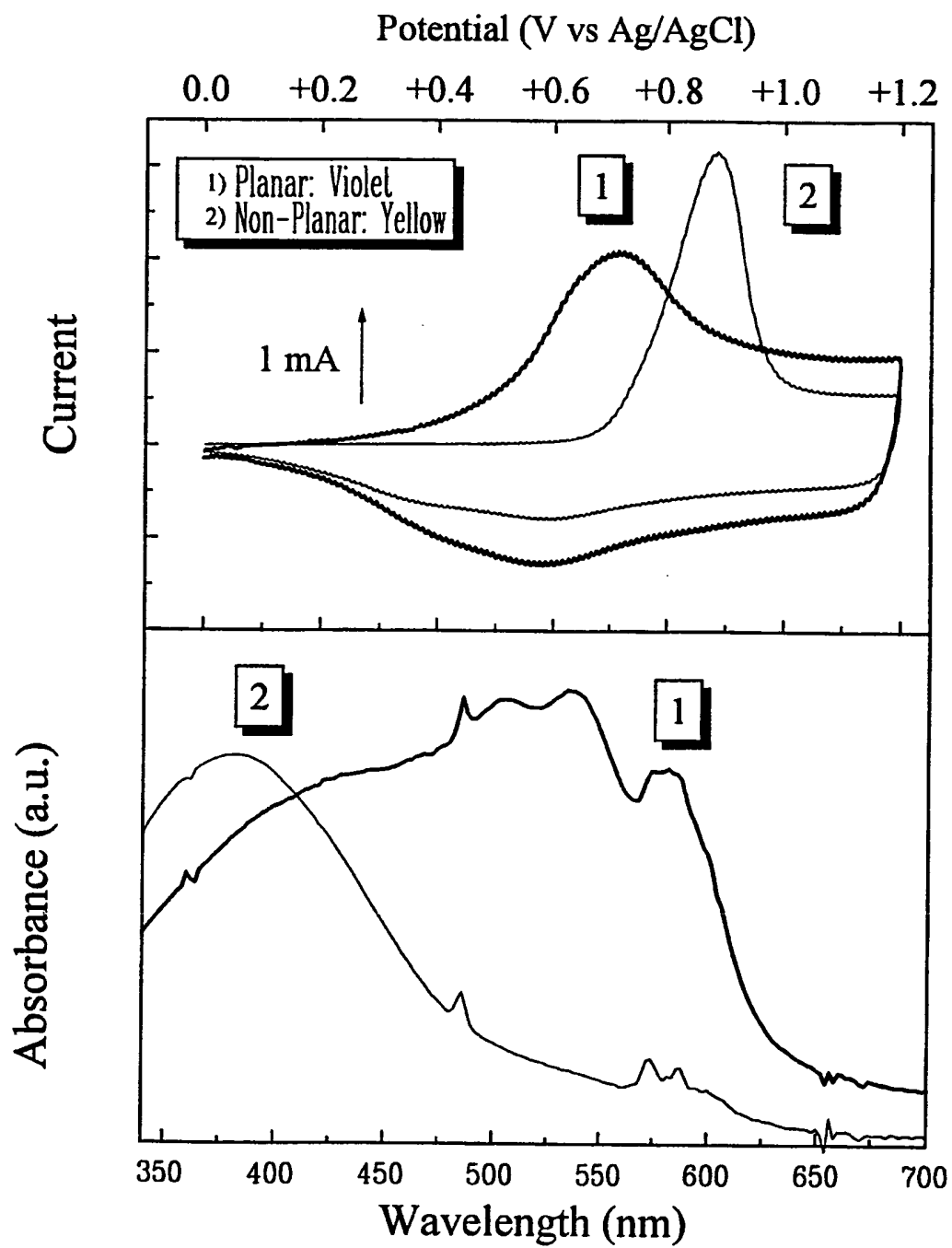
Solid Substrate: Glass, ITO, Gold

FIG. 4

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INTERNATIONAL SEARCH REPORT

Inte. .onal Application No

PCT/CA 98/01082

A. CLASSIFICATION OF SUBJECT MATTER IPC 6 B05D1/18 G01N27/327		
According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) IPC 6 B05D G01N		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practical, search terms used)		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 95 02251 A (MASSACHUSETTS INST TECHNOLOGY) 19 January 1995 see page 17, line 1 - page 20, line 30 ---	1,2
A	EP 0 511 650 A (MATSUSHITA ELECTRIC IND CO LTD) 4 November 1992 see the whole document ---	1
A	US 4 992 300 A (OGAWA KAZUFUMI ET AL) 12 February 1991 see the whole document ---	1
A	US 5 624 711 A (SUNDBERG STEVEN A ET AL) 29 April 1997 see figures 9A,9B ---	1
-/--		
<div style="display: flex; justify-content: space-between;"> <input checked="" type="checkbox"/> Further documents are listed in the continuation of box C. <input checked="" type="checkbox"/> Patent family members are listed in annex. </div>		
<div style="display: flex;"> <div style="flex: 1;"> <p>* Special categories of cited documents:</p> <p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier document but published on or after the international filing date</p> <p>"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p> </div> <div style="flex: 1;"> <p>"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</p> <p>"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone</p> <p>"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.</p> <p>"&" document member of the same patent family</p> </div> </div>		
Date of the actual completion of the international search <div style="text-align: center; font-weight: bold;">12 March 1999</div>		Date of mailing of the international search report <div style="text-align: center; font-weight: bold;">22/03/1999</div>
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016		Authorized officer <div style="text-align: center; font-weight: bold;">Brothier, J-A</div>

INTERNATIONAL SEARCH REPORT

In. stional Application No

PCT/CA 98/01082

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>US 5 338 571 A (MIRKIN CHAD A ET AL) 16 August 1994 see figure 2A</p> <p>-----</p>	1

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/CA 98/01082

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US 5624711 A	29-04-1997	NONE	
US 5338571 A	16-08-1994	NONE	

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